Please cancel claims 2 and 3 without prejudice and amend the claims as follows:

IN THE CLAIMS

1. (amended) An immunogenic conjugate molecule comprising hyaluronic acid moieties covalently bound to an immunologically-suitable polypeptide carrier, wherein greater than about 50% of the hyaluronic acid moieties possess a non-reducing terminal glucuronic acid and/or unsaturated glucuronic acid residue, wherein the hyaluronic acid moieties are low molecular weight hyaluronic acid with a molecular weight of about 400 kD or less and a molecular weight of about 600 daltons or more, and said immunogenic conjugate induces an immune response to epitopes comprising the non-reducing terminal glucuronic acid or unsaturated glucuronic acid residues of said hyaluronic acid moieties.

A1

4. (amended) The immunogenic conjugate according to claim 1, wherein at least 90% of the low molecular weight hyaluronic acid moieties possess a nonreducing terminal glucuronic acid and/or unsaturated glucuronic acid residue.

5. (amended) The immunogenic conjugate according to claim 1, wherein at least 95% of the low molecular weight hyaluronic acid moieties possess a nonreducing terminal glucuronic acid and/or unsaturated glucuronic acid residue.

6. (amended) The immunogenic conjugate according to claim 1, wherein at least 98% of the low molecular weight hyaluronic acid moieties possess a nonreducing terminal glucuronic acid and/or unsaturated glucuronic acid residue.

A2

7. (amended) The immunogenic conjugate according to claim 1, wherein at least 99% of the low molecular weight hyaluronic acid moieties possess a nonreducing terminal glucuronic acid and/or unsaturated glucuronic acid residue.

8. (amended) The immunogenic conjugate according to claim 1, wherein the low molecular weight hyaluronic acid moieties are at least about 4 glycosyl residues in size.

9. (amended) The immunogenic conjugate according to claim 1, wherein the low

molecular weight hyaluronic acid moieties possess about 2 to about 20 disaccharide subunits.

10. (amended) The immunogenic conjugate according to claim 9, wherein the low molecular weight hyaluronic acid moieties possess about 2 to about 10 disaccharide subunits.

11. (amended) The immunogenic conjugate according to claim 1, wherein the polypeptide carrier is selected from the group consisting of tetanus toxoid, diphtheria toxoid, pertussis toxoid, a streptococcal immunogenic polypeptide, an influenzal immunogenic polypeptide, a meningococcal immunogenic polypeptide, a pneumococcal immunogenic polypeptide, and an *E. coli* immunogenic polypeptide.

13. (amended) The immunogenic conjugate according to claim 1, wherein hyaluronic acid moieties are directly linked to the immunologically-suitable polypeptide carrier.

14. (amended) The immunogenic conjugate according to claim 1, wherein the conjugate elicits antibodies that bind an epitope comprising glucuronic acid or unsaturated glucuronic acid as the nonreducing terminal sugar of a low molecular weight hyaluronic acid moiety.

15. (amended) The immunogenic conjugate according to claim 1, wherein the conjugate elicits antibodies that bind capsular hyaluronic acid moieties present in bacteria.

16. (amended) The immunogenic conjugate according to claim 15, wherein the bacterium is group A streptococci or group C streptococci.

19. (amended) A method of preparing a low molecular weight hyaluronic acid moiety – polypeptide conjugate molecule comprising covalently linking low molecular weight hyaluronic acid to an immunologically-suitable polypeptide, wherein about 50% or greater of the low molecular weight hyaluronic acid has a glucuronic acid and/or an unsaturated glucuronic acid residue at the nonreducing terminal.

20. (amended) The method according to claim 19, wherein the method comprising covalently linking a low molecular weight hyaluronic acid to an immunologically-suitable

polypeptide comprises reductive amination.

22. (amended) The purified antibody according to claim 21, wherein the low molecular weight hyaluronic acid moieties are at least about 4 glycosyl residues in size.

23. (amended) The purified antibody according to claim 22, wherein the hyaluronic acid moieties are at least about 4 glycosyl residues and no more than about 40 kD in size.

24. (amended) A pharmaceutical composition effective for treating or inhibiting group A streptococcal or group C streptococcal infection comprising an antibody selected from the group consisting of an antibody elicited by the composition according to claim 17, an antibody according to 21, or an antibody elicited by a low molecular weight hyaluronic acid moiety conjugated to a liposome.

29. (amended) A vaccine comprising the immunogenic conjugate according to claim 3, wherein the vaccine elicits an immune response in humans, said immune response comprising production of anti-low molecular weight hyaluronic acid antibodies.

Please replace the specification as follows:

IN THE SPECIFICATION

Please replace the paragraph on page 17, line 16 through page 18, line 3 with the following:

Hyaluronic acid (100 mg, Lifecore lot 1-9062-5) was added to a 10 ml solution of 0.05 N HCl. The mixture was heated at 80 °C for 2 hours, and stirred in order to dissolve the entire solid. The sample was then heated for another 1.5 hours at 100 °C. The depolymerization was monitored by removal of aliquots from the reaction mixture at various times and analysed on a BIO-RAD system (Biologic) equipped with a Superose® 12 HR 10/30 column (Pharmacia). The solution was neutralized with 0.5 N NaOH, then dialysed with a Diaflo® membrane of

molecular weight cut-off (MWCO) 3,500 and lyophilized. The product was molecular size fractionated through a Superdex® 200 PG (Pharmacia) column to yield 65 mg of solid product. ^{1}H-NMR analysis of the samples at 500 MHz confirmed the structure of the disaccharide-repeating unit of hyaluronic acid (HA). The average molecular weight of the generated fragment was estimated by size-exclusion chromatography coupled with multiangle laser light scattering photometry (SEC MALLS) to be about 12,000 daltons.

On page 18, lines 14-22, please replace the paragraph as follows:

Hyaluronic acid (100 mg, Lifecore lot 1-9062-5) was dissolved in 20 ml of 10 mM PBS buffer, and the suspension stirred until dissolved. The sample was sonicated with a BRANSON sonicator model 450, (sonication settings: Output control: 3; Duty cycle: 50%; temperature: 2 °C) for 18 hours. After dialysis and lyophilization, 57 mg of solid product was recovered. The average molecular weight of the resulting sonicated hyaluronic acid was determined to be 18,000 daltons by SEC-MALLS using a MINIDAWN instrument (Wyatt technology, Santa Barbara, CA) and a Superose® 12 HR 10/30 column (Pharmacia). ^{1}H-NMR analysis of the samples at 500 MHz confirmed the structure of the disaccharide-repeating unit of hyaluronic acid.

Please replace the paragraph on page 19, line 16 through page 20, line 5 with the following:

Periodate-oxidized (d.o. 10% and 20%) acid-treated hyaluronic acid (10 mg of each respectively) and purified tetanus toxoid monomer (5 mg for each sample, Statens Serum Institute, Copenhagen, Denmark) were dissolved in 0.5 mL of 0.2 M sodium phosphate, pH 7.4. Recrystallized sodium cyanoborohydride (10 mg for each sample) was added and the mixture held at room temperature overnight. The progress of the reaction was monitored at various times using a BIO-RAD (Biologic) system equipped with a Superose® 12 HR 10/30 column (Pharmacia). Conjugation of polysaccharide to protein was indicated by a progressive increase of a UV (280 nm) peak eluting in the void volume of the column. After conjugation was completed, 10 mg of $NABH_4$ in 1 ml of 0.1 N NaOH was added to each sample in order to

reduce any remaining unconjugated aldehyde. The conjugate was purified by passage over a column (1.6 x 60 cm) of Superdex® 200 PG (Pharmacia) eluting with 10 mM PBS containing 0.01 percent thimerosal. Fractions corresponding to the void-volume peak were pooled and stored at 4 °C. They were designated conjugates 1 and 2 for 10 and 20 percent oxidation in their polysaccharides, respectively.

On page 20, line 14 through page 21, line 4, please replace the paragraph as follows:

Sonicated and periodate-oxidized HA (7 mg of each sample, d.o. 10% and 20%) and purified tetanus toxoid monomer (3.5 mg for each sample) were dissolved in 350 µl of 0.2 M sodium phosphate at pH 7.4. Sodium cyanoborohydride (7 mg for each sample) was added, and the mixtures held at room temperature overnight. The progress of each conjugation reaction was monitored by removal of aliquots from the reaction mixture at various times and subsequent analysis on a BIO-RAD (Biologic) system equipped with a Superose® 12 HR 10/30 column (Pharmacia). Conjugation of polysaccharide to polypeptide was indicated by the progressive increase of a UV absorbing peak (280nm) eluting in the void volume of the column. After conjugation was completed, $NaBH_4$ (10 mg in 1 ml of 0.1 N NaOH for each sample) was added to the reaction mixtures to reduce any remaining unconjugated aldehyde. The conjugates were purified by passage over a Superdex® 200 PG (Pharmacia) column, eluted with 10 mM PBS containing 0.01 percent thimerosal. Fractions corresponding to the void-volume peak were pooled and stored at 4 °C and were designated conjugates 3 and 4 for 10 and 20 percent oxidation in their polysaccharides, respectively.

Please replace the paragraph on page 21, lines 7-15 with the following:

Sonicated and periodate-oxidized hyaluronic acid (20 mg, 20% d.o.) and rPorB (10 mg) were dissolved in 717 µl of 0.25 M HEPES buffer, pH 8.5, containing 0.25 M NaCl and 0.05 percent ZWITTERGENT Z 3,14 (Calbiochem, San Diego, CA). Sodium cyanoborohydride (20 mg) was added, and the mixture incubated at 37 °C for 1 day. After the conjugation was completed, 10 mg of sodium borohydride in 1 ml of 0.1 N NaOH was added to the reaction

mixture to remove any remaining aldehyde. The conjugate was purified by passage over a column of Superdex® 200 PG (Pharmacia), eluted with 10 mM PBS containing 0.01 percent thimerosal. Fractions corresponding to the void-volume peak, as monitored by UV absorbance at 280 nm, were pooled and stored at 4 °C and labeled as conjugate 5.

On page 22, line 22 through page 23, line 11, please replace the paragraph as follows:

Isolation of the oligosaccharides was performed by anion-exchange chromatography with a MONO-Q HR 5/5 column (Pharmacia) using a HPLC 1090 (Hewlett Packard 1090 Series II) system equipped with a diode-array detector, a programmable auto-injector, a fraction collector, and the Hewlett Packard Chemstation software program for system control and data acquisition/processing. A step-gradient of sodium chloride in Tris-HCL buffer was used for the separation. Two oligosaccharide fractions corresponding to a dimer (DP2) and a tetramer (DP4) eluting, respectively, between 18 to 26 minutes and between 28 to 31 minutes were collected, lyophilized and desalted using a SEPHADEX G-10 column (Pharmacia) and deionized water as eluant. The structure of the oligosaccharides was confirmed by examination of their ^{1}H-NMR spectra at 500 MHz. The DP2 oligosaccharide corresponded to Δ4,5-ß-GlcU-(1,3)-D-GlcNAc, and the DP4 to Δ4,5-ß-GlcU-(1,3)-ß-D-GlcNAc-(l,4)-ß-D-GlcU-(1,3)-ß-D-GlcNAc.

REMARKS

Applicants respectfully request favorable reconsideration in view of the herewith presented amendments and remarks.

Claims 1-33 are pending in this application.

Claims 19-28 and 30-33 are withdrawn from consideration as being directed to non-elected inventions.

Claims 1-18 and 29 are rejected. Please cancel claims 2 and 3 without prejudice.